

WHAT IS CLAIMED IS:

1. A high affinity neutralizing immunoglobulin comprising at least three high affinity complementarity determining regions (CDRs) wherein each said high
5 affinity CDR has an amino acid sequence selected to result in an immunoglobulin with specificity toward at least one antigenic determinant and having an affinity constant (K_a) of at least $10^{10}M^{-1}$ for said antigenic determinant.
2. The high affinity neutralizing immunoglobulin of claim 1 wherein said
10 immunoglobulin comprises at least four high affinity CDRs.
3. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin has 3 high affinity CDRs.
- 15 4. The high affinity neutralizing immunoglobulin of claim 2 wherein said immunoglobulin has 4 high affinity CDRs.
- 20 5. The high affinity neutralizing immunoglobulin of claim 2 wherein said affinity constant (K_a) is at least 10^{11} .
6. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin is specific for at least one protein expressed by a virus.
7. The high affinity neutralizing immunoglobulin of claim 6 wherein said
25 virus is respiratory syncytial virus (RSV).
8. The high affinity neutralizing immunoglobulin of claim 7 wherein the protein is the F protein of RSV.
- 30 9. The high affinity neutralizing immunoglobulin of claim 1 wherein the immunoglobulin has human constant regions.

10. The high affinity neutralizing immunoglobulin of claim 1 wherein the immunoglobulin binds to the same epitope on RSV as the reference immunoglobulin of Figure 1.

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11. The high affinity neutralizing immunoglobulin of claim 1 wherein the immunoglobulin includes framework derived from only a human immunoglobulin.

12. The high affinity neutralizing immunoglobulin of claim 1 wherein at least a portion of the framework is derived from a murine immunoglobulin.

13. The high affinity neutralizing immunoglobulin of claim 1 wherein at least one high affinity CDR contains a phenylalanine residue at a position where a non-phenylalanine residue occurs in the corresponding CDR of the basic or reference antibody of Figure 1.

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14. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin comprises a high affinity H1 CDR and said CDR has an amino acid sequence selected from the group consisting of SEQ ID NO: 9 and 10.

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15. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin comprises a high affinity H3 CDR having the amino acid sequence of SEQ ID NO: 11.

16. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin comprises a high affinity L2 CDR and said CDR has an amino acid sequence selected from the group consisting of SEQ ID NO: 12 and 13.

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17. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin has a high affinity L3 CDR having an amino acid sequence selected from the group consisting of SEQ ID NO: 14, 15 and 16.

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18. The high affinity neutralizing immunoglobulin of claim 1 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 9, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of
5 SEQ ID NO: 4 and the L3 CDR has the amino acid sequence of SEQ ID NO: 14.

19. The high affinity neutralizing immunoglobulin of claim 1 wherein said immunoglobulin has a high affinity L3 CDR having an amino acid sequence selected from the group consisting of SEQ ID NO: 14, 15 and 16.

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20. The high affinity neutralizing immunoglobulin of claim 1 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 9, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of SEQ ID NO: 4 and the L3 CDR has the amino acid sequence of SEQ ID NO: 14.

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21. The high affinity neutralizing immunoglobulin of claim 1 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 9, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of SEQ ID NO: 12 and the L3 CDR has the amino acid sequence of SEQ ID NO: 5.

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22. The high affinity neutralizing immunoglobulin of claim 2 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 10, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of SEQ ID NO: 12 and the L3 CDR has the amino acid sequence of
25 SEQ ID NO: 14.

23. The high affinity neutralizing immunoglobulin of claim 2 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 9, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of
30 SEQ ID NO: 12 and the L3 CDR has the amino acid sequence of SEQ ID NO: 14.

24. The high affinity neutralizing immunoglobulin of claim 2 wherein the H1 CDR has the amino acid sequence of SEQ ID NO: 9, the H3 CDR has the amino acid sequence of SEQ ID NO: 11, the L2 CDR has the amino acid sequence of SEQ ID NO: 12 and the L3 CDR has the amino acid sequence of SEQ ID NO: 15.

25. The high affinity neutralizing immunoglobulin of claim 1 wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 17 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 18.

26. The high affinity neutralizing immunoglobulin of claim 1 wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 19 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 20.

27. The high affinity neutralizing immunoglobulin of claim 2 wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 21 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 22.

28. The high affinity neutralizing immunoglobulin of claim 2 wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 23 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 24.

29. The high affinity neutralizing immunoglobulin of claim 2 wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 25 and the heavy chain variable region has the amino acid sequence of SEQ ID NO: 26.

30. A recombinant high affinity neutralizing immunoglobulin having an affinity constant of at least 10^{10} M^{-1} , wherein said immunoglobulin comprises a human constant region and a heavy and light chain framework region at least part of which is derived from human antibodies.

31. The recombinant high affinity neutralizing immunoglobulin of claim 30 wherein the heavy and light chain framework regions are derived from a consensus sequence of human antibodies.

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32. The recombinant high affinity neutralizing immunoglobulin of claim 30 wherein the affinity constant is at least 10^{11} M^{-1} .

33. The recombinant immunoglobulin of claim 32 wherein the heavy and
10 light chain framework regions are derived from a consensus sequence of human antibodies.

34. A composition comprising the immunoglobulin of claim 1 wherein said immunoglobulin is suspended in a pharmacologically acceptable carrier.

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35. A composition comprising the immunoglobulin of claim 6 wherein said immunoglobulin is suspended in a pharmacologically acceptable carrier.

36. A method of preventing and/or treating a disease comprising
20 administering to a patient at risk thereof, or afflicted therewith, a therapeutically effective amount of the immunoglobulin composition of claim 34.

37. A method of preventing and/or treating a virus-induced disease comprising administering to a patient at risk thereof, or afflicted therewith, a
25 therapeutically effective amount of the immunoglobulin composition of claim 35.

38. A method of preventing and/or treating respiratory syncytial virus comprising administering to a patient at risk thereof, or afflicted therewith, a therapeutically effective amount of the immunoglobulin of claim 7 suspended in a
30 pharmaceutically acceptable carrier.

39. The high affinity neutralizing immunoglobulin of claim 3 wherein said immunoglobulin is selected from the group consisting of Fab, F(ab)'₂, a heavy-light chain dimer, a heavy chain and a light chain.

5 40. The high affinity neutralizing immunoglobulin of claim 4 wherein said immunoglobulin is selected from the group consisting of Fab, F(ab)'₂, a heavy-light chain dimer, a heavy chain and a light chain.

 41. The high affinity neutralizing immunoglobulin of claim 1 wherein said
10 immunoglobulin is an antibody.

 42. The high affinity neutralizing immunoglobulin of claim 2 wherein said immunoglobulin is an antibody.

15 43. The high affinity neutralizing immunoglobulin of claim 6 wherein said immunoglobulin is selected from the group consisting of Fab, F(ab)'₂, a heavy-light chain dimer, a heavy chain and a light chain.

 44. The high affinity neutralizing immunoglobulin of claim 7 wherein said
20 immunoglobulin is selected from the group consisting of Fab, F(ab)'₂, a heavy-light chain dimer, a heavy chain and a light chain.

 45. The high affinity neutralizing immunoglobulin of claim 8 wherein said
25 immunoglobulin is selected from the group consisting of Fab, F(ab)'₂, a heavy-light chain dimer, a heavy chain and a light chain.

 46. A method of preventing and/or treating a disease comprising
administering to a patient at risk thereof, or afflicted therewith, a therapeutically
effective amount of the immunoglobulin of claim 39 or 40 suspended in a
30 pharmaceutically acceptable carrier.

47. A method of preventing and/or treating a virus-induced disease comprising administering to a patient at risk thereof, or afflicted therewith, a therapeutically effective amount of the immunoglobulin of claim 43 suspended in a pharmaceutically acceptable carrier.

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48. A method of preventing and/or treating respiratory syncytial virus comprising administering to a patient at risk thereof, or afflicted therewith, a therapeutically effective amount of the immunoglobulin of claim 44 or 45 suspended in a pharmaceutically acceptable carrier.

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